DOCKET NO.: ISIS-5300 PATENT

Application No.: 10/701,265

Office Action Dated: July 14, 2010

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1-119. (canceled)

120. (currently amended) A composition comprising a duplex consisting of a

first chemically synthesized oligonucleotide and a second chemically synthesized

oligonucleotide, wherein:

each of the first chemically synthesized oligonucleotide and the second chemically

synthesized oligonucleotide independently consists of 17 to 25 linked nucleosides, each

nucleoside comprising a nucleobase and a sugar;

the first chemically synthesized oligonucleotide is 100% complementary to the

second chemically synthesized oligonucleotide and to a target mRNA;

the first chemically synthesized oligonucleotide and the second chemically

synthesized oligonucleotide are not covalently linked to each other; and

the first chemically synthesized oligonucleotide is a gapmer, wherein the gap

comprises at least 4 nucleosides, each comprising a 2'-hydroxy-pentofuranosyl sugar moiety,

and wherein each nucleoside of each wing comprises a 2'-sugar modification; and

the second chemically synthesized oligonucleotide comprises at least one nucleoside

that comprises a 2'-sugar modification.

121. (previously presented) The composition of claim 120, wherein the second

chemically synthesized oligonucleotide is a gapmer, wherein the gap comprises at least 4

nucleosides, each comprising a 2'-hydroxyl pentofuranosyl sugar moiety, and wherein each

nucleoside of each wing comprises a 2' modification.

122-123. (Canceled)

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124. (previously presented) The composition of claim 120, wherein each nucleoside of at least one of the wings of the gapmer comprises a 2' sugar modification selected from fluoro, alkoxy, amino-alkoxy, allyloxy, imidazolylalkoxy, and methoxyethoxy.

125-126. (canceled)

127. (previously presented) The composition of claim 120, wherein each nucleoside of the 3' wing of the gapmer comprises a 2'- OCH₃.

128-135. (Canceled)

- 136. (previously presented) The composition of claim 120, wherein each wing of the gapmer is from two to seven nucleosides in length.
- 137. (previously presented) The composition of claim 120, wherein at least one of the first chemically synthesized oligonucleotide and the second chemically synthesized oligonucleotide comprises at least one phosphorothioate linkage.
- 138. (previously presented) The composition of claim 137, wherein each of the first chemically synthesized oligonucleotide and the second chemically synthesized oligonucleotide comprises at least one phosphorothioate linkage.

139-167. (Canceled)